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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Curtis, Rory A.J.

Serial No.: 09/587,111

Filed: June 2, 2000

For: NOVEL MEMBERS OF THE

CAPSAICIN/VANILLOID RECEPTOR FAMILY OF

PROTEINS AND USES THEREOF

Attorney Docket No.: MNI-062CP2DV1

Commissioner for Patents

Box AF

Washington, D.C. 20231

Certificate of Facsimile Transmission

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Box AF, Washington, D.C. 20231 on the date set forth below.

By:

1103

Date of Signature

Maria Laccorripe Zacharakis, Ph.D.

Group Art Unit: 1646

Examiner: Ulm, J. D.

Attorney for Applicant

Limited Recognition Under 37 C.F.R. 10.9(b)

DECLARATION PURSUANT TO 37 CFR 81.131

Dear Sir:

I, Rory A.J. Curtis, a citizen of the United Kingdom, residing at 78 Hardwick Road,

Ashland, Massachusetts 01721 hereby declare as follows:

Serial Number: 09/587,111

Apr-11-03 03:47pm

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and claimed in the above-identified

Group Art Unit: 1646

- (1) I am the inventor of the subject matter described and claimed in the above-identified application.
- (2) Prior to January 22, 1999, the invention described and claimed in the abovereferenced patent application was completed in this country, as evidenced by the following:

- 2 -

- (a) Prior to January 22, 1999 I had completed the sequencing of the full length human VR-2 (SEQ ID NO:5) as evidenced by copies of the assembled contig map and the complete sequence of SEQ ID NO:5 derived from the contig map. The contig map and sequence print-out are submitted herewith as Exhibits A and B, respectively.
- (b) Prior to January 22, 1999 I had determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor based on the results of a blast search using the amino acid sequence of SEQ ID NO:5. The top hit in this blast search analysis is rat vanilloid receptor I (VR-1; accession number AF029310). Based on the percent identity and percent similarity between the polypeptide of SEQ ID NO:5 and rat VR-1, and the fact that rat VR-1 was the top hit in the blast search analysis I determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor. The results of the blast search analysis are submitted herewith as Exhibit C.
- (c) Prior to January 22, 1999, I had determined that the polypeptide of SEQ ID NO:5 represents a unique target for pain and that it may be responsible for hypersensitivity in chronic neuropathic pain, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule. The Qualified Target Summary Sheet is submitted herewith as Exhibit D.

Serial Number: 09/587,111

- 3 -

Group Art Unit: 1646

(d) According to my toutine practice, immediately after identifying the polypeptide of SEQ ID NO:5 as a vanilloid receptor (hVR-2) associated with pain and classifying it as a Qualified Target, I contemplated routine uses of this molecule such as: (i) use of the molecule in screening assays to identify modulators of the vanilloid receptor or (ii) use of this molecule in the diagnosis of conditions/diseases associated with, for example, aberrant vanilloid receptor (hVR-2) nucleic acid expression or activity, e.g., pain disorders, as evidenced by a copy of the "Qualified Targer Summary Sheet" generated for this molecule.

(e) The dates deleted from the contig map (Exhibit A), the sequence print-out (Exhibit B), the blast search results (Exhibit C), and the Qualified Target Summary (Exhibit D) are prior to January 22, 1999.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

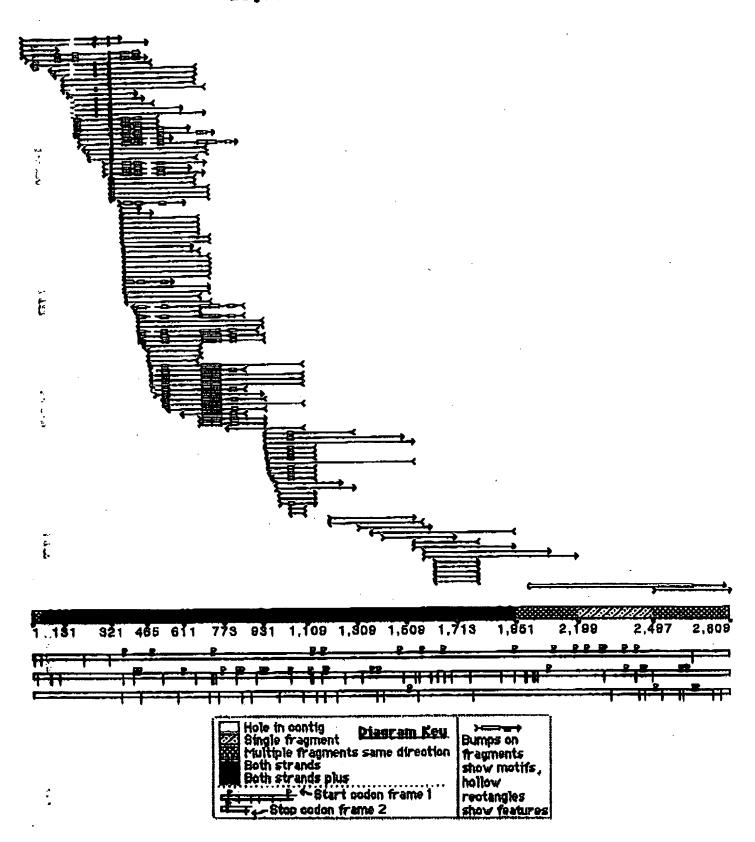
Rong Curts

10/2003

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Exhibit A

21e11a Sequencher "21e11racefinal"



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Exhibit B

21ella Sequencher "21ellracefinal"

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21ella Sequencher "21ellracefinal"

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2 CIDEC2161112 \$411	ADDDTTTAD	gcaggctgec	TCCCATGGAG	TCACAGTGCC	YGGGCGYGGY	CCGGAAATTC	GCCCCCAGA	Targagt	650011001C
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ginkellellhi #290	Adoptetao	SCOGGCTGCC	TCCCATGGAG	#CACAGITCC	YOGGCGYGGY	CCQQAAATTC	Geeecteran	TANGENTER	Cr temperate
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5thea103c2tl 9241	CATTTTQUA	GCGGGCTGCC	TCCCATGGAC	CACACACTEC	AGGGCGAGGA	CCGGAAATT	CTCAGA	TANGAGTCAA	CCTCAACTAC
Genbenk AM- 1230		GCGGGCTGCC					CTCAGA	TANGAGTCAA	OCTCAACTAC
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Christolical. \$193	GATTTTGGGA	OCHGOCTGCC	TCCCATOGAG	TCACAGTTCC	* AGGGCGAGGA	CCGGAAATTC	GCCCCGCAGA	Targagecaa	CCTCAACTAC
Genbank H20_ \$131		cceecrecc							CCTCAACTAC
G-obsok R50- \$130		GCGGGCTGCC					CTCAGA	Targagycaa	CCTCPACTAC
Quebonk 849_ \$130	GATTTTGGCA	GCGGGCTGCC	TCCCATGGA	TCACAGTTCC	ABGCCGAGGA	TTAKADDOO /	etcrga	TARGAGTCAR	CCTCAACTAC
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#3217	TETRAGRADA ACTATOTOCO COTOCAGOTO CTCCAGTOCA ACTGATGGO CAGATGCAGO AGGAGGCAG AGGACAGAGO AGAGGATOTT S R
Achdalell - 9695 frinhlaced - 9205	TCCAACCACA TCTGCTGGCT CTGGGGTCCC AGTGAATTCT GGTGGCAAAT ATATATTTC ACTAACTCAA AAAAAAAAA AAAAAAAA
#2701	THE STREET STREET, STREET, STREET, STREET, STREET, STREET, SCHACTCAL ALALARAMA ANAMANAA
295 295	AAAAAAAA KAAAAAAA
02791	AARAAAAA AAAAAAAA .

Exhibit C

BLASTF vs. PNU (AA) flh21ellorfaa - 5:26:57 pm on Dec 21 98

BLASTP 1 4.10MP-Washu [30-Aug-96] [Build 20:24:58 Oct 21 1996]

Reference: Aluschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search rook, J. Mol. Biol. 215:403-10.

Query= flh21ellorfas (764 letters)

/diskû/asap/databases/db/MRP/protxnu

345,099 sequences; 106,000,184 total letters.

Searching.....done Smallest

Sum Probability High P(N) Score Sequences producing High-scoring Segment Pairs: 1,9e-221 GP:gi 2570933 (AF029310) vanilloid receptor subtype 1 [Ra... 336 9.86-136 6 GPU:gi | 3986159 | gpl | PID | d1035925 (AB015231) VRlsk [Mus mus... 299 6.5e-20 8 GP:gi|2911863 (AF047660) contains similarity to ankyrin r... 203 7 GP:gi | 3675319 | gnl | PID | e1344970 (Z74030) similar to ankyri... 1.1e-19 97 GF:gi 2642590 (AF031408) olfactory channel [Caenorhabditi... 3.6e-16 93 GP:gi 2854148 (AP045639) contains similarity to ankyrin r. GP:gi 3879753 gnl PID el349345 (272514) Similarity to Hum. 4.1e-15 93 3.5e-11 73 2.7=-0B б GP:gi | 3267188 | grl | PID | #315126 (Y10601) ankyrin-like prote... 71 2.2e-05 4 SP:SP:SP | P48994 | TRPL_DROME TRANSIENT-RECEPTOR-FCTENTIAL L... 69 3 5 6e-05 72 GP:gl | 1841966 (U65916) ankyrin [Raccus norvagicus]

WARNING: Descriptions of 4 database sequentes were not reported due to the limiting value of parameter V = 1:

>GP:gi|2570933 (AF029310) vanilloid receptor subtype 1 [Rattus non vagicus] Length = 838

Score = 336 (156.0 bits), Expect = 1.9e-221, Sum F(7) = 1.9e-221Identities = 67/112 (59%). Positives = 84/112 (75%)

206 BYEGELPLSLARCTKQWDVVSYLLENFHQPASLQATDSQGNTVLHALVMISDNSAENIAL 265 Quary:

FYFGELPLSLARCT C +V TLL+N QPA T A DS GNTVLHALV ++DN+ +N

245 PYFGELPLSLAACTNQLAIVKBLLQNSWQPADISARDSVGNTVLHALVEVADNTVDNTKF 304 Sbjct:

266 VTSMYDGLLQAGARLCPTVQLEDIRNLQDLTPLKLAAKEGKIEIFRHILQRE 317 VTSMY+ +L GA+L PT++LE+I N + LTPL LAA GKI + +ILQRE Quexy:

305 VTSMYNEILILGAKLHPTLKLEEITNRKGLTPLALAASSGKIGVLAYILQRE 356 Sbjct:

Score = 316 (146.7 b); Expect = 1.9e-22: Sum P(7) = 1.9e-221 Identities = 65/138 (47%), Positives = 93, 38 (67%)

66 ASQPDPNRBDRDRLFNAVSRGVPEDLAGLFEYLSKTSKYLTDSEYTEGSTGKTCLMKAVL 125 A + P +DR +F+AV++ ++L L +L ++ K LTDSE+ + TGKTCL+KA+L Query:

104 AGEKPFRLYDRRSIPDAVAQSNCQELESLL:PLQRSKKRLTDSEFKDPETGKTCLLKAML 163

Sbjet:

126 NLKDGVNACILPLLQIDRDSGNFQPLVNAQCTDDYYRGHSALHIAIEKRSLQÇVKLLVEN 185 NL +G N I LL + R T + + VNA TD YY+G TALHIAIE+R++ V LLVEN Oneth:

164 NLHNGQNDTIALLLDVARKTDSLKQFVNAS!TDSYYKGQTALHIA:ERRNMTIVTLLVEN 223 Sbict:

185 GANVHARACGRFFQKGQG 203 Query:

. 1

GA+V A A G FF+K +G

224 GADVQAAANGDFFKKTKG 241 Sbacc:

Score = 299 (138 8 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-321

Identifies = 69/175 (39%). Positives = 94/175 (53%)

391 FFLNEICNLIYMPIETAVAYHQPTLKKAAPHLKAEVGNSMLLTGHILILLGGHYLLVGQL 450 lk VG-Query:

434 FYFNFFVYCLYMIIFTAARYYRFVEGLFPYKLKNTVGDYFRVTGEILSVXXXXXXXXXX 493 F+ NF +YM IFTA AY++P Sbjct:

451 WYBWRRHVFIWISFIDSYFEILPLFQALLKPVSQVLCFLAIEWYLPLLVSALPLGWLNLL 510

YF +R + F+DSY EILF Q+L VS VL F + Y+ +V +L +GW N+L Query:

494 QYFLQRRPSLKSLFVDSYSEILPFVQSLF: VSVVLYFSQRKEYVASMVFSLAMGWINML 553 Shict:

511 YYTRGFQHTGIYSVMIQKVILROLLRPLLIYLVFLPGPAVALVSLSQEAWRPEAP 565 Query:

YYTRGFO GIY+VMI+K+ILROL R

Sbjct:

Score = 281 (130.5 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221Identities = 54/95 (56%), Positives = 70/9= (73%)

586 GAQYRGILEASLELFKFTIGMGELAFQEQLHBRGMVLILLLAYVLLTYILLIMMLIALME 645 Query:

G Y + LELFKFTIGMG+L F E P+ + ++LLLAYV+LTYILLINMLIAIM

624 GNSYNSLYSTCLEIBKFTIGMGDLEFTENYDFKAVFIILLLAYVILTYILLLNMLIALMG 683 Sbict:

646 ETVNSVATOSWSIWKLQKAISVLEMENGYWWCRKK 680 Query:

ETVN +A +S +IWKLQ+AI++L+ E + C +K

684 ETVNKIAQESKNIWKLQRAITILDTEKSFLKCMRK 718 Sbict:

Score = 162 (75.2 bits). Expect = 1.9e-221, Sum P(7) = 1.9e-221

Identities = 28/38 (73%). Positives = 34/33 (89%)

323 HLSRKFTEWCYGPVRVSLYDLASVDSCEENSVLBITAF 360 Query:

HLSRKFTEW YGDV SLYDL+ +D+CE+N3VLE+IA+

364 HLSRKFTEWAYGPVHSSLYDLSCIDTCEKNSVLEVIAY 401 Sbjct:

Score = 144 (66.9 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221

Identifies = 25/47 (53%), Posicives = 31/47 (65%)

678 RKKQRAGUMLTVGTKPDGSPDERWCPRVEEVNWASWEQTLPTLCEDP 724 Onery:

RK R+G TL VG FDG D RWCFRV+EVNW +W + + EDP

717 RKAFRSGKILQVGFTPDGKDDYRWCFRVDEVNWTTWNTNVGIINEDP 763 Sbjet:

Score = 94 (43.6 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221

Identities = 15/30 (50%), Positives = 24/30 (80%)

363 KSPHRHRMVVLEPLNKLLQAKWDILLIPKFF 392 Ouery: ++P+RH M+++EPLN+LLQ KWD + + F

405 ETPNRHUMLLVEPLNRLLQDKWDRPVKRIF 434 Sbjct:

Score = 46 (21.4 bits), Expect = 1.3e-162 Sum P(6) = 1.3e-162

Identities = 11/48 (22%), Positives = 24/63 (50%)

435 HILILLGGIYLLUGQLWYFWRRHUFIWISFIDSYFEILFLFCALLKPV 482 Query:

H ++L+ + L+ W + + +B + F+ + I+F

410 HOMLLUBPLINGLLODKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 457 Sbj¢t:

Score = 37 (17.2 bits). Expect = 2.4e-169, Sum P(7) = 2.4e-169

Identities = 3/22 (36%), Positives = 13/22 (59%)

297 PLKLAAKEGKIEIPRHILQREF 318 Query:

PL LAA TT I T TLQ T

251 PLSLAACTNOLAIVKFLLONSW 272 Sbjer:

Score = 37 (17.2 bits), Expect = 1.9e-111, Sum P(7) = 1.9e-111 Id ntities = 8/26 (30%). Positives = 15/26 (57%)

206 FYFGELBLSLAACTKOWDVVSYLLEN 231 Query: TY GT L TA + +VT LTEN 198 YYKGQTALHIAIERRNMTLUTLLUEN 223 Sbjct:

>GPU:g1|3986159|gn1|PID|d1035925 (AB015231) VRlsk [Mus musculus] Length = 563

Score = 289 (138.8 bits), Papect = 9.8e-136, Sum P(6) = 9.8e-136 Identifies = 69/175 (39%), Positives = 94/175 (53%)

391 FFLNFLCNLIYMPIFTAVAYHQPTLKKAAPHLKAEVGNSMLLTCHILILLGGIYLLVGQL 450 LK VG+ +TG IL + Ouery: +YM IFTA AY++P 127 FYFNFFVYCLYMIIFTAAAYYRFVEGLPPYKLKNTVGDYPRVTGEILSVXXXXXXXXXXXII 186

Sbjcr:

451 WYFWRRHUPIWISFIDSYPEILFLFQALLKPVSQVLCFLAIBWYLPLLVSALVLGWLNLL 510 YF TR - P-DSY EILF Q+L VS VL F + YT TV +L TGW N+L Query:

187 QYFLQRRPSLKSLFVDSYSEILFFVQSLFMLVSVVLYFSQRKEYVASMVFSLAMGWINGL 246 Sbjct:

511 YYTRGFQHTGIYSVMIQKVILRDLLRBLLIYLVFLFGFAVALVSLSQEAWRPEAF 565 Query: A+V+L TT

YYTRGSQ GIY+VMI+K+ILRDL R Sbjct:

Score = 253 (117.5 birs), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 50/89 (56%). Positives = 64/89 (71%)

586 GAQYRGILEASLELFKFTIGMGELAFQEOLHFRGMVLLLLLAYVLLTYILLLMALIALMS 645 G Y + LELFKETIGMG+L P E F+ + ++LLLAYV+LTYILLLMMLIALM Quexy:

317 GNSYNSLYSTCLELFKFTIGMGDLEFTENYDFKAVFIIILLAYVILTYILLINMLIALMG 376 Sbjct:

646 ETVNSVATDSWSIWKLQKAISVLEMENGY 674 Ouery: ETV V- -S IWKLQ A TTL++E + 377 ETVGQVSKESKHIWKLQWATTILDIERSF 405 Sbjct:

Score = 163 (75.7 bits). Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 28/47 (59%), Positives = 34/47 (72%)

678 RKKQRAGVMLTVGTKPDGSPDERWCFRVEEVNWASWEQTLPTLCEDP 724 Query: RK R+G M+TVG DG+PD RWCFRV+EVNW+ W Q L - EDP 410 RKAFRSGEMVTVGKSSDGTPDRRWCFRVDEUNWSHWNONLGIINEDP 456 Sbjct:

Score = 163 (75.2 bits). Expect = 9.8e-136, Sum P(6) = 9.8e-136 Identities = 28/38 (73%), Positives = 34/33 (89%)

323 HLSRKFTEWCYGPVRVSLYDLASVDSCEENSVLEIIAF 360 Query: HLSRKFTEW YGPV SLYDL+ +D+CE+NSVLB+IA+ 57 HLSRKFTEWAYGPVHSSLYDLSCIDTCEKNSVLEVIAY 94 Sbjct:

Score = 129 (59.9 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 27/49 (SS%), Positives = 36/49 (73%)

269 MYDGLLQAGARLCPTVQLEDIRNLQDL/TPLKLAAKEGKIEIFRHILQRE 317 Quezy: MY+ +L GA+L PT+TLE+I N + LTPL LAA GKI + +ILQRE 1 MYNEILILGAELHPTLKLEEITNRKGLTPLALAASSGKIGVLAYILORE 49 Sbjct:

Score = 94 (63.6 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136 Identities = 15/30 (50%), Positives = 24/30 (80%)

363 KSPHRHRMVVLBPLNKLLQAKWDLLIPKFF 392

++P+RH M+++EPLN+LLQ KWD + + P 98 ETPNRHDMLLVEFLNRLLQEKWDRFVKRI: 127

Sbjct: Score = 46 (21.4 bits), Expect = 2.3e-77, Sum P(5) = 2.3e-77 Identities = 11/46 (22%), Positives = 24/45 (50%)

435 HILILIGGIYLLVGQLWYFWRRHVFIWISFIDSYFEILFLFQALLKFV 482 H ++L+ + L+ W + + +F + F+ + I+F A +PV Query:

103 HUMILVEPLNRLLQDKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 150 Sbjct:

Score = 42 (19.5 bits). Expect = 1.2e-122. Sum P(6) = 1.2e-122 Identifies = 9/22 (40%), Positives = 16/22 (72%)

209 GELPLSLAACTKQWDVVSYLLE 230 Quexy: G PL-LAA + + V++Y+L+ 26 GLTPLALAASSGKIGVLAYILQ 47 Sbjer:

>GP:gi | 2911863 (AF047660) contains similarity to ankyrin repeats [Caenorhabditis elegans] reudry = 300

Score = 103 (47.8 bits), Expect = 6.5e-20 Sum P(8) = 6.5e-20 Identities = 23/89 (25%), Positives = 44/89 (49%)

497 LLVSALVIGWLNILYYTRGFQHTGTYSVMIQKVILRDLLRFLLIYLVELFGFAVALVSLS 556 L+ ++ ++ LYY R + G + +M+ +I D+ RF+LIY +PL GF+ + Greil:

592 LITVIMIFTTVHYLYYCRVIRFVGPFVLMVYTIIATDIFRFMLIYGIPLMGFSQSFSLIF 651 Sbjct:

557 QEAWRPEAPTGPNATESVQPMEGQEDEGN 585 Onsky: T+ + EG +++ N 652 LSCEREANVIKKLITDQSEASEGSDNKFN 680 Sbjct:

Secre = 63 (29.3 bits), Expent = 6.5e-20, Sum P(8) = 6.5e-20Identities = 15/27 (55%), Positives = 18/27 (66%)

291 MLQDLTPLKLAAKEGKIEIFRHILQRE 317 Query: N Q L+PL LAAK K E+F IL+ E 328 NKQSLSPLTLAAKLAKKEMPDEILELE 354 Sbjct:

Score = 56 (26.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20 Identities = 16/48 (33%), Positives = 25/:2 (52%)

151 LVNAQCTODYYRGHSALHIAIEKRSLQCVALLVENGANVHARACGR\$P 158 Onery: + V ++ GA+V++R G FF + + G S LH AI 185 LLNDIHISPDFYGLSPLHOAIINTDCKLVYKFLKLGADVNSRCYGAFF 232 L+N Sbjet:

Score = 54 (25.1 bits). Expect = 6.5e-20. Sum, P(8) = 6.5e-20Identities = 12/25 (52%), Positives = 13/23 (56%)

207 YFGELPLSLAACTKQWDVVSYLL 229 Onera: Y GE PLS AAC Q + LL 263 YLGEYPLSBAACLNOPESPRLLL 285 Sbjet:

Score = 49 (22.8 bits), $2 \times pecc = 6.5e-20$, Sum P(8) = 6.5e-20 Identities = 8/23 (344), Positives = 12/23 (52%)

331 WCYGPVRVSLYDLASVDSCRENS 353 Onera: TYLA -D+ E+ W YG 359 WAYGDASSTAYPLAKIDTINETT 381 Sbict:

Score = 47 (21.8 bits), Expect = 6.5e-20, $\lim_{n \to \infty} P(8) = 6.5e-20$ Identities = 11/30 (36%), Positives = 18/.3 (60%)

236 ASLQATOSOGNTVLHALVMISCNSAENIAL 265 Onera: A+ A D+ GN+VLH V+ ++ 289 ANPNAODTNGNSVLHMCVIHENMAMBKLAL 318

sbjct:

Score = 46 (21.4 bits). Expect = 5.7e-15. Sum P(6) = 5.7e-13 Identities = 9/27 (33%), Positives = 17/27 (52%)

163 GHSALHIAIEKRSLQCVKLLVENGANV 189 Query: G+S LH+ + ++ KL +E GA++ 298 GNSVLEMCVIHENMAMFKLALECGASL 324 Sbict:

Score = 43 (20.0 bits). Expect = 6.56-20. Sum P(8) = 6.5e-20 Identities = 8/18 (44%), Positives = 13/18 (72%)

634 ILLLMMLIALMSETVNSV 651 Query: I+ NMLIA+M+ T TT 753 IMQFNMLIAMMTRTYETI 770 Sbje:

Score = 41 (19.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20 Identities = 10/27 (37%). Positives = 16/27 (59%)

113 GSTGKTCLMKAVLNLKDGVNACILELL 139 Query: GS G+T + +L+ D NA +L +L 153 GSMGETIIGCCLLHASDIHNALVLKIL 179 Sbjer:

Score = 35 (16.3 bits). Expect = 0.00016, Sum P(3) = 0.00016 Identities = 9/37 (24%). Positives = 16/37 (43%)

67 SQPDPMRFDRDRLFWAVSRGVPEDLAGLPEYLSKTSK 103 Query: GT E+ S-P P R+ TT V + 464 SEPFPGRYCKNSTLQQVKPVINATSRGLVEWSEPLSC 500 Sbjck:

Score = 34 (15.8 bits), Expect = 6.8e-11, Sum P(8) = 5.8e-11Identities = 8/31 (25%). Positives = 17/31 (54%)

422 LKAEVENSMLLTGHILILLGGIYLLVGQLWY 452 Greta: L ++ +L+ ++LI + I+ V L+Y 577 LACDLSPVLLVVDNVLITVTMIFTTVHYLY: 607 Sbjct:

>GP:gi|3675319|gnl|FID|e1344970 (274030) similar to ankyrin repeats [Caenorhabditis elegans] >GP:gi|3876480|gnl|PID|el346172 (272508) simular to ankyrin repeats [Caenorhabditis elegans] Length = 790

Score = 97 (45.0 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 18/53 (33%). Positives = 32/53 (60%)

497 LLVSALVLGWINLLYYTRGFOHTGIYSVMIQXVILRDLLRFLLIYLVFLFGFA 549 + + +++L + LYY R G + +M+ +I DL+RF +IY +FL GF+ 526 MAIISILLUTOHFLYYMRAIPFVGPFVLMVYTIIATDLVRFAMIYSIFLVGFS 578 Sbjct:

Score = 89 (41.3 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 19/48 (39%). Positives = 27/48 (56%)

151 LVNAQCTDDYYRGHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198 Query: L+N C + Y G S LH+AI + Q LL+ GA+++ R G FF 189 LINDICVSEPYYGLSPLHLAIVNQDAQFTS). LRLGADLNQRCYGAFB 236 Shick:

Score = 62 (28.8 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 13/23 (56%). Positives = 14/23 (60%)

207 YFGELPLSLARCTKOWDVVSYLL 229 Ouery:

YEGE PLS A C Q D+ LL

267 YFGEYPLSFAICMGOHDLFRMLL 289 Sbict:

Score = 51 (23.7 bits), Expect = 1.le-19, Sum P(7) = 1.le-19

Identicies = 10/19 (52%), Positives = 13/19 (68%)

236 ASLQATDSQGNTVLHALVM 254 Onery:

A+L A D+ GNT LH V+

293 ANLSAODTMONTALHLOVI 311 Sbjct:

Score = 49 (22.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19

Identities = 11/51 (21%), Posicives = 27/51 (52%)

601 KPTIGNGELAFOEOLHFRGMVLILLLAYVLLTYILLLNMLIALMSETVNSV 651 Ouery:

IL N+LIA+M+ T ++ E++ + ++ L+ ++

626 EFSVLYREMSACONFWMKWIGKLIFVIFET/ SILOFNLLIAMMTRTYETI 676 Sbjet:

Score = 43 (20.0 birs). Expect = 1.2e-06, Sum P(5) = 1.2e-06

Identities = 7/27 (25%), Positives c 16/27 (59%)

163 GHSALHIAIEKRSLQCVKLLVENGANV 189 Onera:

G++ALH+ + + + ++E G N+

302 GNTALHICVIHOKMDMLDAVLEAGGNI 328 Sbjct:

Score = 39 (18.1 bits), Expect = 5.5e-12, Sum P(7) = 5.5e-12

Identities = 12/56 (21%). Positives = 25/56 (44%)

461 WISFIDSYPEILFLFQALLKFVSQVLCBLAIEWYLPLLVSALVLGWINLLYYTRGF 516 Query:

W TFT ++ L AL T TC LA ++ L + TTTL TT F

483 WFNFLKAPPAKLMFKGABLFIIISIPCRLACSFHEFFLTIDNTMAIISILLVTOHF 538 Sbjc::

Score = 38 (17.6 bits), Expect = 1.1e-19, Sim P(7) = 1.1e-19 Identifies = 9/18 (50%), Positives = 12/18 (66%)

289 IRNLQDLTPLKLAAKEGK 306 Overy:

+ N Q+LT L LAA+ K

330 LANKONLTALTLAARLAK 347 Sbjct:

Score = 37 (17.2 bits). Expect = 4.7e-18. Sum P(7) = 4.7e-18 Identities = 7/15 (46%), Positives = 9/15 (60%)

Query: 723 DPSGAGVPRTLENPV 737

+ENPV DP G+

Sbjet: 599 DPMGSEPNNIMENPV 613

Score = 36 (16.7 bits), Expect = 1.1e-19, Sum F(7) = 1.1e-19

Identities = 10/47 (21%), Positives = 16/47 (34%)

376 LNKLLQAKWDLLIPKFFLNFLCNLIYMFIBTAVAYHQPTLKKAAPHL 422 Orgen:

TL L IT + AY + ++L KW

362 IEQILDEKWKAYGRALWLRSLLGFIFFYCCFVCAYMLRPSSATTEHL 408 Sbjct:

Score = 35 (16.3 bits). Expect = 3.0e-08, fin P(5) = 3.0e-08

Identities = 9/23 (39%), Fosicives = 11/23 (47%)

207 YFGELPLSLAACTKOWDVVSYLL 229 Query:

Y+G PL LA + S LL

199 YYGLSPLHLATVNQDAQFTSLLL 221 Sbjet:

Score = 34 (15.8 bits), Expect = 3.9e-12, Sum P(5) = 3.9e-12

Identities = 7/21 (33%), Positives = 13/21 (61%)

Query: 297 PLKLAAKEGKIEIFRHILQRE 317
PL A G+ ++FR +L ++
Sbjct: 272 PLSFAICMEQHDLFRMLLAKK 292

Score = 34 (15.8 bits), Expect = 8.9e-10, Sum P(7) = 8.9e-10

Identities = 6/18 (33%), Positives = 12/18 (66%)

Query: 610 AFQEQLHPRGMVLILLLA 627 AF +L P+G L ++++ Sbjct: 489 AFPAKLMFKGAPLFIIIS 506

Score = 34 (15.8 bits), Expect = 4.0e-08, Sum P(6) = 4.0e-08Identities = 11/40 (27%), Positives & 16/40 (40%)

Query: 153 Naoctodyyrghsalhiaiekrslocvklivenganvhar 192 N T Y G L AI ++L+ AN+ A+ Sbjcc: 259 Ntnytgsmyfgeyplspaicmgohdlfrmllakkanlsag 298

Sbjct: 259 NTNYTGSMYFGEYFLSFAIC MCQalles Attended 250

>GP:gi|2642590 (AF031408) olfactory channel [Caenorhabditis elegans] Length = 937

Score = 93 (43.2 bits), Expect = 6.8e-16, Sum P(5) = 5.8e-16 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 CHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198
G SALH+AI + V LL+ + A+V+ARACG FF
Sbjct: 172 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 207

Score = 92 (42.7 bits), Expect = 6.8e-16, Sum P(5) = 6.8e-16 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMICKVILRDLLRFLLIYLVFLFGFA 549
L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+
SDjct: 500 LFVFALFGSWIFLLFBARSAKLTGFFVQMIYSMIAGDMIRFAIISAIFLVSFS 552

Score = 57 (26.5 bits). Expect = 6.8e-16. Sum P(5) = 6.8e-16 Identities = 10/24 (41%). Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230
Y+GE FL+ AAC D+ L++
Sbjcl: 226 YYGEYFLAFAACFGNKDIYDLLIQ 249

Score = 50 (23.2 bits), Expect = 6.8e-16, Sum P(5) = 5.8e-16 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAAKPGKIEIPRHILQ 315 N TPL LA K G+ +IF +L+ Sbjct: 294 NHAGFTPL/LATKLGRKQIFEPMLE 318

Score = 44 (20.4 bits), Expect = 5.8e-16. Lam P(5) = 6.5e-16 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 Degentulhalumisoneaenial 265 De entelh Vt +e + &t Sbjet: 258 Defentilhmcvinysesmysyau 281

Score = 37 (17.2 bits), Expect = 2.2e-05. Sum P(4) = 2.2e-05. Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 PGELPLSLAACTKQWDVVSYLLEN 231
FG+ L LA ++ VS LL +
Sbjct: 171 FGQSALHLAIVHDDYETVSLLLNS 194

Score = 34 (15.8 bits), Expect = 3.6e-16, Sum P(6) = 3.6e-16 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384 +P M+ E + +LL KW Sbjor: 363 TPEHLDMIGSEVIQRLLADKW 383

>GP:gi|2654148 (AF045639) contains similarity to ankyrin repeats [Caenorhabditis elegens] Length = 957

Score = 93 (43.2 bits), Expect = 7.6e-16, Sum F(5) = 7.6e-16 Identities = 19/36 (52%), Positives = 25/36 (59%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 196 G SALH+AI + V LL+ + A-V+ARACG FF Sbict: 175 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 210

Score = 92 (42.7 bits), Expect = 7.6e-16. Sum P(5) = 7.6e-16 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLMLLYYTRGFQHTGIYSVMIQKVILRDLIRFLLIYLVFLFGFA 549

L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+

SDJCt: 503 LEVPALPGSWIFLLFFARSAKLTGPFVQMIYSMIAGDMIRFAIISAIFLVSFS 555

Score = 57 (26.5 bits). Expect = 7.6e-16, Sam P(5) = 7.6e-16 Identities = 10/24 (41%), Positives = 15/2: (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230
Y+GE PL+ AAC D+ L++
Sbjct: 229 YYGEYPLAFAACFGNKDIYDLLIQ 252

Score = 50 (23.2 bits), Expect = 7.6e-16, Sum P(5) = 7.6e-16Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAAKEGKIEIPRHILQ 315 N TPL LA K G+ +IF +L+ Sbjet: 297 NHAGFTPLTLATKLGRKQIFEEMLE 321

Score = 44 (20.4 bits), Expect = 7.5e-16, Sum P(5) = 7.6e-16 Identities = 10/24 (41%), Positives = 15/24 (52%)

Query: 242 DSQGNTVLHALVMISDNSAENIAL 265 DS GNT+LH V+ +S + A+ Sbjct: 261 DSFGNTILHMCVINYSSSMYSYAV 284

Score = 37 (17.2 bits), Expect = 2.4e-05, Sum P(4) = 2.4e-05Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231
FG+ L LA ++ VS LL +
Sbjet: 174 FGQSALHLAIVHDDYETVSLLLNS 197

Score = 34 (15.8 bits). Expect = 4.1e-16. Sum P(6) = 4.1e-16 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPINKLLQAKW 384 +P M+ 2 - +LL KW Sbjct: 366 TPEHLDMIGSEVIQRLLADKW 386 >GP:gi|3879753|gn1|PID|el349345 (272514) Similarity to Human ankyrin (SW:ANK1_HUMAN) [Caenorhabditis elegans]
Length = 519

Score = 73 (33.9 bits). Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 17/36 (47%), Positives = 19/36 (52%)

Query: 163 GHSALHIAIRKRSLQCVKLLVENGANVHARACGRFF 198 C S LH AI L+ V L GA+VH R G FF Sbjct: 186 GLSPLHQAIVMEDLEMVYFLCRKGADVHQRCYGSFF 221

Score = 63 (29.3 bits). Expect = 3 6e-11, Sum P(6) = 3.6e-11 Identities = 12/17 (70%), Positives = 13/17 (76%)

Query: 207 YFGELPLSLAACTKQWD 223 Y+GE PLS AACT Q D Sbjct: 252 YWGEYFLSBAACTNQVD 268

Score = 52 (24.1 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 13/27 (48%), Positives = 17/27 (62%)

Quary: 289 IRNLODLTPLKLAAKEGKIEIFRHILC 315 +RN LTPL LAA+ K I+ IL+ Sbjct: 315 VRNNLKLTPLALAARLAKKHIYDLILE 341

Score = 51 (23.7 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11Identities = 10/22 (45%), Positives = 12/22 (54%)

Query: 331 WCYGPVRVSLYDLASVDSCEEN 352 W YGPV Y L VD+ E+ Shlet: 348 WRYGPVVCKAYPLNDVDTINES 369

Score = 43 (20.0 bits). Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 8/13 (61%), Positives = 10/13 (76%)

Query: 242 DSQGNTVLHALVM 254 D+ GNTVLH V+ Sbjet: 284 DINGNTVLHLTVI 296

Score = 37 (17.2 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 8/35 (223), Positives = 16/35 (45%)

Query: 376 LNKILCAKWDLLIPKFFLNFLCNLIYMFIF VAY 410 + ++L+KW+ K L TY +A+ Sbjet: 398 IEEVLESKWETFGKKQLFMSLAGYIYFLAVFYLAF 432

>GP:gi|3287188|gnl|PID|e315126 (Y10601) ankyrin-like protein [Homo sapiens]
Length = 1119

Score = 71 (33.0 bits). Expect = 2.7e-08, Sum P(6) = 2.7e-08 Identities = 13/30 (43%). Positives = 20/30 (66%)

QUETY: 163 GHSALHIAIEKRSLQCVKLLVENGANVHAR 192 G++ LH A+EK ++ VK L+ GAN + R Sbjct: 98 GNTPLHCAVEKNQIESVKFLLSRGANPNLR 127

Score = 63 (29.3 bits). Expect = 2.7e-08. Sum P(6) = 2.7e-08 Identities = 10/30 (33%), Positives = 20/30 (66%)

Query: 501 ALVLGWLNLLYYTRGFQHTCIYSVMIQKVI 530
A+ W+N L Y + F++ GI+ VM++ ++

Sbjct: 838 AVYPYWMN9LLYLQRPENCGIFIVMLEVIL 367

6177424214

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Score = 59 (27.4 bits), Expect = 9.0e-07, Sim P(6) = 9.0e-07 Identities = 10/30 (33%), Positives = 19/30 (63%)

Query: 167 LHIAIERRSLQCVKLLVENGANVHARACGR 196 LH+A++ L+ +K+ ++NGA + 243 LHLAVONGDLEMTIONCLONGAQIDPVEKGR 272 Sbjct:

Score = 50 (23.2 bits), Expect = 2.7e-08, Sum P(E) = 2.7e-08Identities = 10/26 (38%), Positives = 18/26 (69%)

291 NLQDLTFLKLAAKEGKIEIFRHILQR 316 Query: TL +TPL LAAK G TT T TLTT 479 DLHGMTPLHLAAKNGHDKVVQLTLKK 504 Sbjct:

Score = 49 (22.8 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08Identities = 10/25 (38%), Positives = 14/26 (53%)

209 GELPLSLAACTKQWDVVSYLLENPHQ 234 G PL LA + W++V+ LL 342 GRSPLILATARASWNIUNLLLSKGAQ 367 Sbjct:

Score = 48 (22.3 bits). Expect = 3.2e-05, Sum P(5) = 3.2e-05 Identities = 9/32 (26%), Positives = 20/32 (62%)

524 VMIQKVILRDLLRFLLIYLVFLFGFAVALVS.. 555 OnerA: THE TUILT LLR THAT L F TH 860 IVMLEVILKTLLRSTVVFIFLLLAPGLSFYIL 891 Sbjct:

Score = 41 (19.0 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08Identicies = 9/28 (32%), Positives = 15/28 (53%)

525 MIQKVILRDLLRFLLIYLVFLFGFAVAL 552 Query: +IR+LR + P+ + LF F + L 865 VILKTILRSTVVFIFILIAPGLSFYILL 892 Sbjct:

Score = 40 (18.6 bits), Expect = 2.9e-07, Sum P(5) = 2.9e-07 Identities = 13/50 (26%). Positives = 24/50 (48%)

620 MVLLLLLAYVLLTYILLINMLIALMSETVNSVATDSWSIWKLQKAISVLE 665 +V + LL L++ +LLN+ S ++ < T S T + Query: 875 WFIFLILAPGLSFYILINLODPFSSPLLSIIQTFSMMLGDIMYRESFLE 924 Sbjct:

Score = 40 (18.6 bits), Expect = 7.6e-05, Sum P(5) = 7.6e-05Identifies = 8/19 (42%), Positives = 12/19 (63%)

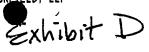
296 TPLKLAAKEGKIPIFRHIL 314 Query: TPL LA + G +B+ + L 241 TPLHLAVQNGDLEMIKMCL 259 Shict:

Score = 39 (18.1 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08 Identities = 7/19 (36%). Positives = 14/19 (73%)

625 LLAYVLLTYILLIMMLIAL 643 CHEIN: I+L+N+LI L L-++ T 941 LUSFTIFUPIVLMNLLIGL 959 Sbjct:

Score = 39 (18.1 bits). Expect = 6.8e-07, Sum P(6) = 6.8e-07Identifies = 9/36 (25%). Positives = 18/36 (50%)

293 QDLTFLKLAAKEGKIEIFRHILQREFSGLSHLSRKF 328 CHELY: - LT L '- +IE+ H + +E+ + L+ E 681 EPLTAL NAMVQNNRIELLNHPVCKEYLLMKW.AYGF 716 Sbjet:





Qualified Target Summary Sheet

	Vanilloid Receptor Homologue
	(VR-2)
FA Disease Area (8):	Pain
druggable Target Class:	Calcium channel
MPI Gene Sequence Identifier:	Flh21e11 (Mine 18560)
Top Blast Hit:	Rat vanilloid receptor 1 (VR1)
Amino Acid Coding Region:	ORF: 361-2652
CDNA Length:	2806 bp
Source (Tissue / Cell Line):	First clone identified in an internal heart library
	? Unrecognized / Novel
Novel / Unrecognized: % Novelty:	66% novel across the complete cDNA. Hits unannotated sequence in Non-Public Patent Data Base
Patent Status:	Filed Nov. 1, 1998
Full Length Clone:	Yes
Expression Profiling Results:	Present in a sub-population of sensory neurons different from VR1. Also present in sympathetic neurons.
Background:	The published vanilloid receptor (Caterina et. Al. Nature 389:816-24, 1997) responds to heat and capsaicin by activating Ca++ influx in sensory neurons (Tominaga et.al., Neuron 21: 531-43, 1998). Capsaicin also binds to this channel.
Hypothesis:	This channel may be responsible for hypersensitivity in curding neuropathic pain and represents a unique target for pain.
Assay Type:	Cell-based assay
Reagents Needed:	Open reading frame will be cloned by Millennium into pCDNA 3.1
Readout:	
Critical Experiments Necessary:	

MPI Target Name:

QT Nomination Date:

Action Taken:

Date Accepted: Bayer QT Leader: MPI QT Leader:

Vanilloid Receptor Homologue (VR-2)

12/22/98

Accepted QT (unrecognized) Pending full length cDNA

Rory Curus or Peter DiStefano

Confidential: QT-0002 (VR-2)

BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE UNITED STATE PATENT AND TRADEMARK OFFICE

From-LAHIVE & COCKELELD, LLP

LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)

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Expires: August 5, 2003

Harry I. Moatz

Director of Enrollment and Discipline